IRIS Document

CRAVE Notes.	1987/12/02	Assessment Record	79
Chemical Name	Document Date YYYY MM DD	File Descriptor	Sequence #

IRIS FILE TYPE

Circle One → IRIS Chemical File

Public Submission

RfD/RfC & CRAVE Files

Subtype

Circle One

Decision files for chemicals listed in IRIS

Chemical nominations

CRAVE files prior to 1995

Toxicological Review

New Information

Non-decisional file reference and supplemental date prior to 1997

Peer review Record

Other

Key/difficult to find materials

Other

Other

RfD / RfC Meeting Notes

Description

EPA

Organization

Rita Schoeny

Author

Scan Date

Hatleson

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF RESEARCH AND DEVELOPMENT
ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
CINCINNATI, OHIO 45268

December 8, 1987

SUBJECT: Notes of 12/2/87 Meeting

FROM: Rita Schoeny
Environmental Criteria and Assessment Office

TO: CRAVE Work Group

In attendance were the following:

L.Anderson
A. Bathija
D. Beal
A. Chiu
L. Cullen
H. Gibb
D. Guth
C. Hiremath
E. Margosches
R. McGaughy
Y. Patel
J. Quest
C. Ris
R. Rubenstein
R. Schoeny
D. Wellington

1. A status table (Att. 1) was distributed. Please note that the benzene summary will be included on IRIS before the public release.

2. Individuals preparing summary sheets were reminded to cite specific references for all statements made on the sheets. This applies also to information given in the Supporting Data section. It was also requested that copies of any papers thus cited which were not in the literature file be sent to R. Schoeny.

3. The question was raised as to how to deal with compounds which are contaminated with or associated with agents of a different classification (see 2,4,5-(trichlorophenoxy) propionic acid and pentachloronitrobenzene). It was decided to remark on these situations in a brief note separate from but immediately following the classification statement.

4. A discussion was held on the appropriateness of using split classifications (eg. B2/C). See Attachment 2 for notes.

5. Chemical Specific Issues

ACROLEIN CAS: 107-02-8

C, possible human carcinogen

The classification was found acceptable. CAG pointed out that a more recent EPA document exists than those cited; namely a 1987 Health Effect Assessment document (HEA). This refers to a paper by Lijinsky which is described in the animal data section. CAG will supply a copy of this paper to ECAO. The animal data section will be revised to include a more complete description of the skin-painting and subcutaneous injection studies as well as the arguments for considering the study on glycialdehyde. Supporting data will be revised to include structural relationship to other carcinogens.

ASBESTOS CAS: 1332-21-4

A human carcinogen.
Slope factor, oral = 1.4 E-3/fibers/L based on NTP (1985) benign epithelial neoplasms in male F344 rats; slope factor, inhalation = 2.3 E-1/fibers/ml.

The classification had been accepted at the 9/15/87 meeting. Further modifications to the human data section will include revision of the paragraph on ecologic studies in drinking water to conform to the Drinking Water Criteria document. This will involve a review of the Marsh (1983) paper. H. Gibb will supply comments in this regard.

It was decided to defer discussion of the oral quantitative estimate until ECAO has completed revisions to the DWCD.

The inhalation quantitative estimate was found to be appropriate. The sheet will be modified to include the human data summary supplied by OAQPS. The classification and inhalation estimate sections were agreed to be suitable for inclusion on IRIS after the suggested modifications.

PENTACHLORONITROBENZENE CAS: 82-68-8

C, possible human carcinogen

The subject of discussion was whether to consider the pure compound or a technical mixture which is contaminated with other chloronitrobenzenes and chlorinated benzenes. OPP will supply a recent PD-2 describing this issue. Also pertinent to the classification is the type of carcinogenic response induced by hexachlorobenzene. After distribution of this information and revision of the summary sheet, pentachloronitrobenzene will be rescheduled.

2-(2,4,5-TRICHLOROPHENOXY) PROPIONIC ACID CAS: 93-72-1

D, not classified as to human carcinogenicity.

There was consensus on this classification. The following note will be added after the classification statement: NOTE: Commercial 2,4,5-TP contains 2,3,7,8-tetrachloro-p-dioxin, a known animal carcinogen.

XYLENES (Technical Grade Mixture) CAS: 1330-20-7

D, not classified as to human carcinogenicity.

As xylenes are generally encountered as a mixture of isomers the above designation and CAS number will be used on IRIS.

As there was a well-run NTP (1986) bioassay which apparently achieved MTD and no increased tumor incidence in rats or mice, it was questioned whether the classification should be E, evidence of non-carcinogenicity. There is cited a study by Maltoni which reported an increase in total tumors as a consequence of xylene exposure. It was decided to obtain this paper and any other information which would assist in evaluation and to reconsider the compound for an E classification at a later date. The ODW document manager for xylenes will be queried as to whether the SAB considered the E classification.

Table 1

OPTS			R. Hill	N
	OTS		Margosches	N
		HERD	Beal, Cullen	N
	OPP		Farber	N
			Quest	N
ORD	ORS		Preuss	
	OHEA	CAG	McGaughy	Y
			Gibb	Y
			Chen	Y
			Farland	Y
		ECAO	Schoeny	N
		FORUM	Bellin	
	OHR	HERL	Nesnow	
OW	ODW		Anderson	N
OAR	OAQPS		Guth, Cote	N
OSWER	OSW		Rubensten, Bathija	N
OPRM	OPPE		Wellington	Y as guidelines are now N with improvement of guidelines

Work Group Member: Herman Gibb

Program Office: CAG (ORD)

X Split Classifications (eg. B2/C) are acceptable.

_____ Split Classifications are not acceptable.

Comments:

There are situations where a chemical may not fully meet the criteria of a particular classification but do satisfy criteria which are alone that of a lower classification. If one opts for either the lower or higher classification than the risk manager might seriously be misled. To choose one or the other for the convenience of the manager does a disservice to the scientific aspect of the classification. There is no question that picking one or the other makes it easier for the manager but the question one must ask oneself is "Is this classification reflective of what we know about the chemical?"

11/9/87

Work Group Member: DIANE D BEAL

Program Office: OTS

_____ Split Classifications (eg. B2/C) are acceptable.

__✓__ Split Classifications are not acceptable.

Comments:

1. IT IS THE RESPONSIBILITY OF THE CRAVE TO MAKE A CLEAR RECOMMENDATION TO THE REGULATORY OFFICES AS TO IF THE CHEMICAL SHOULD BE TREATED AS A PROBABLE OR ONLY A POSSIBLE HUMAN CARCINOGEN.

2. THE TECHNICAL PANEL THAT DEVELOPED THE CLASSIFICATION GUIDELINES RECOGNIZED THAT THERE WAS A GRADATION OF EVIDENCE WITHIN EACH CATEGORY AND CHOSE NOT TO SUBDIVIDE EACH CATEGORY OR TO SPLIT CLASSIFICATIONS. A THINK THAT A DECISION TO SPLIT CLASSIFICATIONS SHOULD ONLY BE MADE BY THAT TECHNICAL PANEL, IF DEEMED NECESSARY BY CRAVE AT ALL.

3. I HAVE MET WITH THE OTHER MEMBER OF CRAVE FROM OPTS (ELIZABETH MARGOSCHES, DICK HILL AND JACK QUEST). WE ALL AGREE THAT A SPLIT CLASSIFICATION IS NOT ACCEPTABLE.

Work Group Member: LARRY ANDERSON

Program Office: ODW

_____ Split Classifications (eg. B2/C) are acceptable.

__✓__ Split Classifications are not acceptable.

Comments: ODW position that has been explained repeatedly — B2 = it is, C = it isn't, B2/C = we are not sure = not useful for regulation

Work Group Member: Robert E. McGaughy 11/19/87

Program Office: ORD/OHEA/CAG

✓ Split Classifications (eg. B2/C) are acceptable.

_____ Split Classifications are not acceptable.

Comments:

They are useful in communicating to the program office that the chemical doesn't fit into either of the two classifications, on scientific grounds alone. The program office will have to deal with that uncertainty.

This problem is <u>not</u> the same as deciding whether or not it is a carcinogen, as some think. Only A's are carcinogens and only E's are not carcinogens.

Work Group Member: Reva Rubenstein / Ambika Balluja

Program Office: OSW

_____ Split Classifications (eg. B2/C) are acceptable.

✓ Split Classifications are not acceptable.

Comments:

If CAG cannot make up their minds about classification, CRAVE Work Group should decide on the classification.

Work Group Member: Elizabeth Margosches

Program Office: OTS

_____ Split Classifications (eg. B2/C) are acceptable.

X Split Classifications are not acceptable.

Comments:

Diane Beal (OTS) and I met with Karl Baetcke (OTS). Diane polled Reto Engler (OPP); we briefly talked with Jack Quest (OPP). I think we're all in agreement.

Work Group Member: Dan Guth

Program Office: OAR

_____ Split Classifications (eg. B2/C) are acceptable.

X Split Classifications are not acceptable.

Comments:

The matter of split classifications was discussed with 8 members of the Pollutant Assessment Branch, OAQPS. The predominant view is that split classifications would not be helpful to OAR programs. Reasons for this view include:

- perceived inconsistency between program offices
- split classifications would place the responsibility for a risk assessment decision on the risk managers.
- The current classification scheme should be maintained and CRAVE should resolve any "disputes".

Two people felt that split classifications would be acceptable because the PAB currently performs a case-by-case analysis for toxic air pollutants.

Status of CRAVE Work Group Outputs
INTERNAL USE ONLY-DO NOT CITE OR QUOTE

CHEMICAL NAME	CAS #	MEETINGS STATUS	UNIT RISK ORAL (/ug/L)	UNIT RISK INHALATION (/ug/cu.m)	CLASS
Acrylonitrile	107-13-1	02/11/87 IR 03/17/87	1.5E-5	6.8E-5	B1
Aldrin	309-00-2	03/05/87 IR	4.9E-4	4.9E-3	B2
Benzidine	92-87-5	12/17/86 IR	6.7E-3	6.7E-2	A
Benzo[a]pyrene	50-32-8	01/07/87 IR	NA	NA	B2
Bis(chloroethyl)ether	111-44-4	07/23/86 IR	3.3E-5	3.3E-4	B2
Butadiene-1,3	106-99-0	01/07/87 IR	NA	2.8E-4	B2
Cadmium	7440-43-9	11/12/86 IR	NA	1.8E-3	B1
Carbon Tetrachloride	56-23-5	11/12/86 IR 12/04/86	3.7E-6	1.5E-5	B2
Chlordane	57-74-9	04/01/87 IR	3.7E-5	3.7E-4	B2
Chloromethyl Methyl Ether	107-30-2	05/13/87 IR	NA	NA	A
Chromium(VI)	7440-47-3	06/26/86 IR	NA	1.2E-2	A
Dibutylnitrosamine	924-16-3	07/23/86 IR 08/13/86 10/29/86	1.6E-4	1.6E-3	B2
Dichloroethane-1,2	107-06-2	12/04/86 IR	2.6E-6	2.6E-5	B2
Dichloroethylene-1,1	75-35-4	12/04/86 IR 01/07/87	1.7E-5	5.0E-5	C
Diethylnitrosamine	55-18-5	07/23/86 IR 08/13/86 10/29/86	4.3E-3	4.3E-2	B2
Dimethylnitrosamine	62-75-9	08/13/86 IR 10/29/86	1.4E-3	1.4E-2	B2
Diphenylhydrazine-1,2	122-66-7	07/23/86 IR	2.2E-5	2.2E-4	B2
Epichlorohydrin	106-89-8	08/13/86 IR	2.8E-7	1.2E-6	B2
Heptachlor	76-44-8	04/01/87 IR	1.3E-4	1.3E-3	B2
Heptachlor Epoxide	1024-57-3	04/01/87 IR	2.6E-4	2.6E-3	B2

Status of CRAVE Work Group Outputs
INTERNAL USE ONLY-DO NOT CITE OR QUOTE

CHEMICAL NAME	CAS #	MEETINGS STATUS	UNIT RISK ORAL (/ug/L)	UNIT RISK INHALATION (/ug/cu.m)	CLASS
Hexachlorobutadiene	87-68-3	11/12/86 IR	2.2E-6	2.2E-5	C
Hexachlorocyclohexane, technical	none-001	12/17/86 IR	5E-5	5E-4	B2
Hexachlorocyclohexane-alpha	319-84-6	12/17/86 IR	1.8E-4	1.8E-3	B2
Hexachlorocyclohexane-beta	319-85-7	12/17/86 IR 03/05/87	5.3E-5	5.3E-4	C
Hexachlorocyclohexane-delta	319-86-8	12/17/86 IR	NA	NA	D
Hexachlorocyclohexane-epsilon	6108-10-7	12/17/86 IR	NA	NA	D
Hexachlorodibenzo-p-dioxin (57653-85-7)	19408-74-3	01/07/87 IR	1.8E-1	1.3E-6	B2
Hexachloroethane	67-72-1	07/23/86 IR	4.0E-7	4.0E-6	C
Methylene Chloride	75-09-2	12/04/86 IR	2.1E-7	4.1E-6	B2
N-Nitroso-N-methylethylamine	10595-95-6	02/11/87 IR	6.3E-4	NA	B2
N-Nitrosodi-N-propylamine	621-64-7	02/11/87 IR	2.0E-4	NA	B2
N-Nitrosodiethanolamine	1116-54-7	02/11/87 IR	8.0E-5	NA	B2
N-Nitrosodiphenylamine	86-30-6	02/11/87 IR	1.4E-7	NA	B2
N-Nitrosopyrrolidine	930-55-2	07/23/86 IR 10/14/86	6.1E-5	6.1E-4	B2
Nickel Carbonyl	13463-39-3	04/01/87 IR	NA	NA	B2
Nickel Refinery Dust	00-02-0	04/01/87 IR	NA	2.4E-4	A
Nickel Subsulfide	12035-72-2	04/01/87 IR	NA	4.8E-4	A
Radon 222	14859-67-7	12/17/86 IR	1.8E-6/pci/L	NA	A
Tetrachloroethane-1,1,2,2	79-34-5	06/26/86 IR	5.8E-6	5.8E-5	C
Trichloroethane-1,1,2	79-00-5	07/23/86 IR	1.6E-6	1.6E-5	C
Trichloroethylene	79-01-6	12/04/86 IR	3.2E-7	1.3E-6	B2
Trichlorophenol-2,4,6	88-06-2	06/26/86 IR	5.7E-7	5.7E-6	B2
Uranium	7440-61-1	12/17/86 IR	5.6E-6/pci/L	NA	A

SUMMARIES VALIDATED, NOT YET ON IRIS

11/30/87

Status of CRAVE Work Group Outputs
INTERNAL USE ONLY-DO NOT CITE OR QUOTE

CHEMICAL NAME	CAS #	MEETINGS STATUS	UNIT RISK ORAL (/ug/L)	UNIT RISK INHALATION (/ug/cu.m)	CLASS
Alachlor	15972-60-8	04/01/87 V 04/22/87	1.7E-6	NA	B2
Aldicarb	116-06-3	08/05/87 V 08/26/87	NA	NA	D
Aniline	62-53-3	05/13/87 V			
Benzene	71-43-2	07/23/86 V 11/09/87	7.4E-6	7.4E-6	A
Bis(2-ethylhexyl)phthalate	117-81-7	08/26/87 V 10/07/87	2.4E-6	NA	B2
Butyl Benzyl Phthalate	85-68-7	08/26/87 V	NA	NA	C
Chloroform	67-66-3	11/12/86 V 12/04/86 12/17/86 08/26/87	1.7E-7	2.3E-5	B2
Copper	7440-50-8	09/15/87 V	NA	NA	D
Creosote	8001-59-8	05/13/87 V	NA	NA	B1
DDD	72-54-8	06/03/87 V 06/24/87	6.9E-6	NA	B2
DDE	72-55-9	06/24/87 V	9.7E-6	NA	B2
DDT	50-29-3	11/12/86 V 06/24/87	9.7E-6	9.7E-5	B2
Dibutyl Phthalate	84-74-2	08/26/87 V	NA	NA	D
Dichloropropene, 1,3- (Telone II)	542-75-6	02/11/87 V 03/05/87	1E-5	NA	B2
Dicofol	115-32-2	06/03/87 V 06/24/87 08/05/87	1.2E-5	NA	C
Dieldrin	60-57-1	03/05/87 V	4.6E-4	4.6E-3	B2
Diethyl Phthalate	84-66-2	08/26/87 V	NA	NA	D
Dimethipin (Harvade)	55290-64-7	11/10/87 V	NA	NA	C

Status of CRAVE Work Group Outputs
INTERNAL USE ONLY-DO NOT CITE OR QUOTE

CHEMICAL NAME	CAS #	MEETINGS STATUS	UNIT RISK ORAL (/ug/L)	UNIT RISK INHALATION (/ug/cu.m)	CLASS
Dimethyl Phthalate	131-11-3	08/26/87 V	NA	NA	D
Dimethyl Sulfate	77-78-1	05/13/87 V	NA	NA	B2
Ethylbenzene	100-41-4	10/07/87 V	NA	NA	D
Ethylene Dibromide	106-93-4	04/22/87 V 05/13/87	1.9E-3	2.2E-4	B2
Folpet	133-07-3	10/07/87 V	3.5E-3	NA	B2
Fomesafen	72128-02-0	08/05/87 V	5.4E-6	NA	C
Furmecyclox	60568-05-0	06/24/87 V 08/05/87	8.6E-7	NA	B2
Hydrazine, Hydrazine Sulfate	302-01-2	05/13/87 V 06/03/87	8.5E-5		B2
Methoxychlor	72-43-5	10/07/87 V	NA	NA	D
Metolachlor	51218-45-2	11/10/87 V	NA	NA	C
N-Nitroso-N-ethylurea	759-73-9	01/07/87 V	NA	NA	B2
N-Nitroso-N-methylurea	684-93-5	01/07/87 V	NA	NA	B2
Oryzalin	19044-88-3	10/07/87 V 11/10/87	NA	NA	C
Paraquat	1910-42-5	10/07/87 V	NA	NA	C
Parathion	56-38-2	08/05/87 V	NA	NA	C
Pentachlorophenol	87-86-5	11/10/87 V	NA	NA	D
Polychlorinated Biphenyls	1336-36-2	04/22/87 V	2E-4	NA	B2
Radium 226,228	7440-14-4	12/17/86 V	3.6E-5/pci/L	NA	A
Styrene	100-42-5	04/01/87 V 11/09/87	8.6E-7	5.7E-7	B2
Toluene	108-88-3	09/15/87 V	NA	NA	D
Toxaphene	8001-35-2	03/06/87 V	3.1E-5	3.1E-4	B2
Trichloroethane-1,1,1	71-55-6	08/05/87 V	NA	NA	D

Status of CRAVE Work Group Outputs
INTERNAL USE ONLY-DO NOT CITE OR QUOTE

CHEMICAL NAME	CAS #	MEETINGS STATUS	UNIT RISK ORAL (/ug/L)	UNIT RISK INHALATION (/ug/cu.m)	CLASS
Trifluralin	1582-09-8	05/13/87 V 06/03/87 06/24/87	2.2E-7	NA	C

Status of CRAVE Work Group Outputs
INTERNAL USE ONLY-DO NOT CITE OR QUOTE

CHEMICAL NAME	CAS #	MEETINGS STATUS	UNIT RISK ORAL (/ug/L)	UNIT RISK INHALATION (/ug/cu.m)	CLASS
Hexachlorocyclohexane-gamma	58-89-9	02/17/86 RE 02/11/87 03/05/87 09/15/87	3.8E-5	3.8E-4	C
Tetrachloroethylene	127-18-4	12/04/86 RE	1.5E-2	4.8E-7	C

Status of CRAVE Work Group Outputs
INTERNAL USE ONLY-DO NOT CITE OR QUOTE

CHEMICAL NAME	CAS #	MEETING DATES	ISSUES TO BE RESOLVED
Pentachloronitrobenzene	82-68-8	11/10/87	Whether to use quantitative risk estimate in 1986 HEEP.
Tetrachlorodibenzo-p-Dioxin-2,3,7,8	17-46-016	04/22/87	TCDD is being reevaluated by CAG as to its mechanism of action as a carcinogen.
Vinyl Chloride	75-01-4	08/13/86	Feron data to be reevaluated by CAG. Data of Hong et al. to be discussed for use in inhalation estimate.

Status of CRAVE Work Group Outputs
INTERNAL USE ONLY-DO NOT CITE OR QUOTE

CHEMICAL NAME	CAS #	MEETING DATES	ISSUES TO BE RESOLVED
Acrylamide	79-06-1	10/29/86	Finalization of OTS document.
Allyl Chloride	107-05-1	11/12/86	Slope factor to be recalculated.
Asbestos	1332-21-4	09/15/87	Inhalation estimate needs further review. Some question as to how ODW wishes to evaluate for oral route.
Beryllium	7440-41-7	04/01/87	Reschedule after SAB review.
Bis(chloromethyl)ether	542-88-1	07/23/86	Slope factor to be recalculated.
Chlordimeform	6164-98-3	04/22/87	OPP will evaluate new human exposure data.
DBCP	96-12-8	09/15/87	Need update on metabolism and incidence data for oral study. Need comment on underestimation of inhalation risk.
Dichlorobenzene-p	106-46-7	10/29/86	Finalization of OTS document.
Dichlorobenzidine	91-94-1	07/23/86	Data from NTP bioassay to be evaluated.
Dichloropropane 1,2-	78-87-5	11/10/87	CAG will redo calculations incorporating life table adjustment.
Dinitrotoluene-2,4	121-14-2	04/01/87 04/22/87	Recent study by CIIT on 2,6-dinitrotoluene must be evaluated. ECAO will contact HEEP author.
Dioxane-1,4	123-91-1	05/13/87	CAG will recalculate slope factor with adjustment for early mortality.
Ethylene Oxide	75-21-8	10/29/86	Evaluation of NTP bioassay to be done by CAG.
Fluridone	59756-60-4	11/10/87	Committee had question regarding MTD in mice. Problems regarding biological significance of skin tumors in female mice, and trend for mononuclear leukemias in rats.
Hexachlorobenzene	118-74-1	08/13/86	Complete Lambrecht report to be obtained. ECAO will check on availability of Turkish epidemiology data.
Nitropropane-2	79-46-9	08/26/87	Should classification be B or C; CAG is re-evaluating data from OTS.

ADDRESSEES

P. Preuss (Chair)

L. Anderson
A. Bathija
D. Beal
J. Bellin
C. Chen
L. Cullen
T. Farber
W. Farland
H. Gibb
D. Guth
R. Hill
R. Kimbrough
R. McGaughy
E. Margosches
R. Picardi
J. Quest
A. Revesz
R. Rubenstein
D. Wellington

ATTACHMENT 2

NOTES ON DISCUSSION OF SPLIT CLASSIFICATION

Memos were sent to all CRAVE Work Group members to solicit opinions from them as well as the policy of their program office on the subject of split classifications. This designation, namely a B2/C, had been applied to Lindane (γ-hexachlorocyclohexane) on the basis that available evidence for carcinogenicity did not allow the compound to be placed definitively in either category B2 or C. The replies of the work group members are listed in Table 1. Following that table are comments sent in by individuals.

Generally, program office representatives saw the use of split classifications as not useful and possessing the potential for confusion. If a split classification were used, the situation could easily arise that Program Office 1 would regulate the agent as B and Program Office 2 as C. It was stated by several representatives that it is our job both as Agency scientists in risk assessment and as members of the CRAVE to make these decisions and not to put this responsibility on risk managers.

Members of the CAG argued that use of the split classification provides an additional tool in describing the risk assessment and in educating risk managers or other persons using the risk assessment as to the uncertainties involved.

It was generally agreed that describing the risk and all the issues involved in determining the weight of evidence is an integral part of our responsibility. It was also generally accepted that the carcinogenicity guidelines are in need of some modification. In the interim, it was suggested that we not use a new classification that is not described in the published guidelines; i.e., B2/C.

Our recommended procedures is as follows. The Program Office, CAG or other group in the Agency applies the Guidelines to available evidence for carcinogenicity of an agent and produces their best scientific judgement as to the classification. If the scientists can not assign the agent into a particular class, they will communicate this to the Work Group at the time of the CRAVE review. The Work Group members will not vote on the classfication but rather will attempt to reach consensus based on an examination of the data. If the CRAVE cannot come to a resolution, Work Group members will identify the issues involved, prepare documentation to that effect and ask the Risk Assessment Forum assemble a technical panel to render a decision.

After the CRAVE has had an opportunity to review and comment upon the foregoing, memos will be sent to the Program Office and other interested parties (eg. head of OHEA) requesting that split classifications not be proposed in Agency documents. A memo will also be sent offering the assistance of the CRAVE in the process of re-evaluating the carcinogenicity guidelines.